Other

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PTO-1590 (9-90)

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Requestor's		1468 Kenr	Serial Number:	09/768.	417,9
Date:	10/21/27/202	Phone: 305-	122 757 6	Art Unit: 1/65	2
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=> D HIS L100-L108

(FILE 'HCAPLUS' ENTERED AT 14:31:54 ON 27 DEC 2002)

FILE 'REGISTRY' ENTERED AT 14:57:31 ON 27 DEC 2002

1 S 389085-38-5 25 S 46.150.18/RID AND 591.385.57/RID AND 4432.3.25/RID 25 cpds 25 S 46.150.18/RID AND JOIL.
24 S L101 NOT L100 24 Csnb tract out applicants) L101 L102

FILE 'HCAPLUS' ENTERED AT 14:59:50 ON 27 DEC 2002

6 S L102 6 cites L103 12885 S DIMERIZATION+NT/CT SO S DIMERIZATION+NT/CT

BO S DEXAMETHASON?

BO S METHOTREXAT?

BO S L104 AND L105 AND L106

C S L107 NOT L103 no Al. Sites L104 27680 S DEXAMETHASON? L105 11846 S ?METHOTREXAT? L106 L107

0 S L107 NOT L103 no other cites L108

> RID = ring identifies (46.150. 18/rid = [0] 591.385.57/rid = [0] | 4432. 3. 25/rid =

these 3 ring systems must be in the Same cpd, connected in any manner w) any o then atoms. pretty broad-but only 25 gpds (LIOI)

KERR 09/768,479

=> D QUE L103 L100 1			389085-38-5
L101 25	SEA FILE=REGISTRY ABB=ON	PLU=ON	46.150.18/RID AND 591.385.57/
	RID AND 4432.3.25/RID		
	SEA FILE=REGISTRY ABB=ON		
L103 6	SEA FILE=HCAPLUS ABB=ON	PLU=ON :	L102

=> d ibib abs hitstr 1

L103 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS 2002:869480 HCAPLUS ACCESSION NUMBER:

137:334940

DOCUMENT NUMBER: Covalent chemical inducers of protein dimerization and TITLE:

their uses in high throughput binding screens

Cornish, Virginia W. INVENTOR(S):

PATENT ASSIGNEE(S): USA

U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. SOURCE:

Pat. Appl. 2002 59,272.

CODEN: USXXCO

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002168685 US 2002168737 ORITY APPLN. INFO.	A1 A1	20021114 20021114	5 2001 /004/1 112	20020124 20010124 20010124

PRIORIT MARPAT 137:334940

OTHER SOURCE(S): Described are compds. having the formula: where H1 is a substrate capable of selectively binding to a first receptor; where H2 is a substrate capable of selectively binding to and selectively forming a covalent bond with a second receptor; and wherein Y is a moiety providing a covalent linkage between H1 and H2, which may be present or absent, and when absent, H1 is covalently linked to H2. Also described are uses of the compds. for in vivo screening of compds. and proteins. In this compd., the 1st ligand-receptor pair is replaced with a small mol.-receptor pair that will form an irreversible covalent linkage, making a system with only 3 non-covalent interactions. Such an approach allows for the screening of small mols. to identify their cellular targets. This covalent system is used for screening the ligand receptor interaction, which used to require laborious work by using the photo cross linking, radio labeled ligand binding and affinity chromatog. techniques.

351419-43-7, L-Homocysteine, N-[4-[[(2,4-diamino-6-IT pteridinyl)methyl]methylamino]benzoyl]-S-[8-[[2-[[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-methyl-3oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]octyl]-351419-44-8, L-Homocysteine, N-[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]-S-[10-[[2-[[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-methyl-3oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]decyl]-443985-11-3, L-Homocysteine, N-[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]-S-[3-[[2-[[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-methyl-3oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]propyl]-443985-12-4, 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]amino]-1-

oxobutyl]amino]ethyl]thio]methyl]-7-[[7-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17yl]carbonyl]amino]-1-oxoheptyl]amino]-8-oxo-, (6R,7R)- 443985-13-5

, 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]amino]-1-

oxobutyl]amino]ethyl]thio]methyl]-7-[[8-[[(11.beta.,16.alpha.,17.alpha.)-

9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17-

yl]carbonyl]amino]-1-oxooctyl]amino]-8-oxo-, (6R,7R)-

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (covalent chem. inducers of protein dimerization and uses in high throughput binding screens)

RN

CN

L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[8-[[2-[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]octyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[10-[[2-[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-RN methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]decyl]-CN (9CI) (CA INDEX NAME)

L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy l]-S-[3-[[2-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-RN methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]propyl]-CN (9CI) (CA INDEX NAME)

RN 443985-12-4 HCAPLUS

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

5-[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6-3-[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino]-1-oxobutyl]amino]ethyl]methyl]methyl]-7-[[7-[[(11.beta.,16.alpha.,17.alpha.)-oxobutyl]amino]ethyl]thio]methyl]-7-[[7-[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17-NAME)

RN 443985-13-5 HCAPLUS

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-63-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino]-1pteridinyl)methyl]methyl]amino]-1oxobutyl]amino]ethyl]thio]methyl]-7-[[8-[[[(11.beta.,16.alpha.,17.alpha.)oxobutyl]amino]ethyl]thio]methyl-3-oxoestra-1,4-dien-179-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17yl]carbonyl]amino]-1-oxooctyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

=> d ibib abs hitstr 2

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L103 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
                        2002:696096 HCAPLUS
ACCESSION NUMBER:
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DOCUMENT NUMBER:

137:197882

TITLE:

Three hybrid assay system

INVENTOR(S):

Becker, Frank; Come, John H.; Kley, Nikolai

PATENT ASSIGNEE(S):

Gpc Biotech Ag, Germany; Gpc Biotech Inc.

SOURCE:

PCT Int. Appl., 253 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.			KI	KIND DATE APPLIC				ATION NO.			DATE					
2002	02070662			A2 20020912												
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The invention concerns compns. and methods for isolating ligand binding AΒ polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. In general the invention provides a three hybrid assay system and reagents for the identification of the protein binding partner of a selected small pharmaceutical agent. Likewise, the invention also provides methods and reagents for the identification of a small pharmaceutical agent binding partner of a selected protein. Once detected, the invention further provides methods for monitoring the interaction of the pharmaceutical agent and its protein binding partner that can be used to detect competitors of the interaction.

452913-18-7P 454221-45-5P, GPC 285937 IT RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses) (three hybrid assay system)

452913-18-7 HCAPLUS RN

L-Glutamine, N2-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-CNN-[13-[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-methyl-3oxoandrosta-1, 4-dien-17-yl]-13-oxo-3, 6, 9-trioxa-12-azatridec-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

454221-45-5 HCAPLUS RN CN

5,8,11-Trioxa-2,14-diazanonadecan-19-oic acid, 18-[[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]amino]-1-[(11.beta., 16.alpha., 17.alpha.) -9-fluoro-11, 17-dihydroxy-16-methyl-3oxoandrosta-1,4-dien-17-yl]-1,15-dioxo-, (18S)- (9CI) (CA INDEX NAME)

PAGE 1-B

=> d ibib abs hitstr 3

L103 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:575201 HCAPLUS

137:121947 DOCUMENT NUMBER:

Covalent chemical inducers of protein dimerization and TITLE:

their uses in high throughput binding screens

Cornish, Virginia W. INVENTOR(S):

The Trustees of Columbia University In the City of New PATENT ASSIGNEE(S):

York, USA

PCT Int. Appl., 98 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PATENT NO.	KIND DATE	APPLICATION NO. DATE								
	WO 2002059272	A2 20020801	WO 2002-US2199 20020124								
	rata TATE TAC	ατ. αν απ. αυ.	AZ, BA, BB, BG, BR, BY, BZ, CA, Ch, CN,								
	CO CD	CII CZ DE DK.	DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,								
	GM, HR,	HU, ID, IL, IN,	IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,								
	LS, LT,	LU, LV, MA, MD,	MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,								
	PL, PT,	RO, RU, SD, SE,	SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,								
		US, UZ, VN, YU,	ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,								
	TJ, TM	T.C. NEI ME	CD CI CZ TZ IIG ZM ZW. AT. BE, CH,								
	RW: GH, GM,	KE, LS, MW, MZ,	SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,								
	CY, DE,	DK, ES, FI, FK,	GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG								
	BF, BJ,	CF, CG, CI, CM,	GA, GN, GQ, GW, FILL, FI								
	US 2002168/3/	A1 20021114	US 2001-768474 20010124 US 2001-768474 A2 20010124								
	RITY APPLN. INFO).:	having the formula: H1-Y-H2 where H1 is a								
AB	The invention C	concerns compas.	y binding to a first receptor; where H2 is								
		of coloctiv	ralty hinding to and selectively lorming a								
	2 (1,	ith a cocond rec	confore and wherein i is a molecy providing								
	2 1 2 - 1	are between HI and HV which may be bresent or absent, a									
	han abaant Ul	l is covalently l	inked to HZ. Also described are uses or								
	the compde for	r in vivo screen:	ing of compas. are proteins. In this								
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	3	anim that will fo	orm an irreversible covalent linkage, making								
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	and and austom is used for screening the ligand receptor interaction,										
	which used to require laborious work by using the photo closs linking,										
	radio labeled ligand binding and affinity chromatog. techniques.										
ΙT											
11	4400F 40 4 4420F 12-F										
	Dr DDC /7-51-11	tigal reagent use	e); ANST (Analytical study); USES (Uses)								
	(covalent cl	hem. inducers of	protein dimerization and uses in high								
	,										

throughput binding screens)

351419-43-7 HCAPLUS RN

L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy CN 1]-S-[8-[[2-[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]octyl]-(9CI) (CA INDEX NAME)

351419-44-8 HCAPLUS

RN $L-Homocysteine, \ N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino] benzoy \\$ CN 1]-S-[10-[[2-[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]decyl]-(9CI) (CA INDEX NAME)

RN 443985-11-3 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[3-[[2-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]propyl]- (9CI) (CA INDEX NAME)

RN 443985-12-4 HCAPLUS

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-1-oxobutyl]amino]ethyl]thio]methyl]-7-[[7-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17-yl]carbonyl]amino]-1-oxoheptyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

RN 443985-13-5 HCAPLUS

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-1-oxobutyl]amino]ethyl]thio]methyl]-7-[[8-[[((11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoestra-1,4-dien-17-yl]carbonyl]amino]-1-oxooctyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

KERR 09/768,479

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L103 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: . 2002:31914 HCAPLUS

DOCUMENT NUMBER: 136:98820

DOCUMENT NUMBER: 130:98820

TITLE: Yeast three-hybrid system for in vivo drug screening

and enzyme evolution using chemical inducers of

dimerization

INVENTOR(S): Cornish, Virginia W.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S.

Ser. No. 490,320.

CODEN: USXXCO

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 2002004202 A1 20020110 US 2001-768479 20010124

PRIORITY APPLN INFO: US 2000-490320 A2 20000124

PRIORITY APPLN. INFO.: US 2000-490320 A2 20000124 The disclosed invention relates to the evolution of enzymes in vivo, and drug screening in vivo through the use of chem. inducers of protein dimerization. The subject invention provides a compd. having the formula: H1--X--B-Y--H2 wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage or bond formation, comprising the steps of: (a) providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout; (b) providing the compd. of the invention which dimerizes the pair of fusion proteins, said compd. comprising two portions coupled by a bond that is cleavable or formed by the protein to be screened; and (c) screening for the cellular readout, wherein a change the cellular readout indicates catalysis of bond cleavage or bond formation by the protein to be screened. However, it has not heretofore been suggested to use small mol. induced protein dimerization to screen for catalysis in vivo., and specifically, it has not been suggested to use an enzyme cleavable moiety to link two mols. to dimerize proteins. This invention provides proteins de novo with prescribed binding and catalytic properties and permits screening cDNA libraries based on biochem. function. Practically, we believe that powerful screens in combination with existing randomization techniques will make it possible to take an existing protein fold and evolve it into an enzyme with a new function generating useful catalysts for the pharmaceutical and chem. industries. Since the screen is done in vivo and in both prokaryotes and eukaryotes, the methodol. can be applied to functional genomics and drug discovery. A new chem. inducer of dimerization (CID) was recently developed in Professor Cornish's lab, which uses a heterodimer of methotrexate (MTX) and dexamethasone (DEX) which, when placed in the yeast three-hybrid system, reconstitutes transcription of the lacZ gene. The effects of altering the structure of the DEX-MTX CID and the protein chimeras in the three-hybrid assay were investigated. It was obsd. that all DEX-MTX CIDs, except the DEX-MTX CID with the shortest chem. linker, showed the ability to induce .beta.-galactosidase levels at levels 400% above strains possessing no CID. The DEX-MTX CIDs showed little or no increase in

.beta.-galactosidase levels above background levels in strains where dihydrofolate reductase (DHFR) from E. coli was replaced by DHFR from murine. The three-hybrid system did show some directional preference to the way in which the receptors where fused to the DNA binding domain and the activation domain. These studies have led to a better understanding of the factors that are important in activating transcription in the DEX-MTX yeast three-hybrid system.

IT 389085-33-0 389085-34-1 389085-35-2 389085-36-3 389085-37-4 389085-39-6 389085-41-0 389085-42-1

RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(yeast three-hybrid system for in vivo drug screening and enzyme evolution using chem. inducers of dimerization)

RN 389085-33-0 HCAPLUS

CN

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
3-[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-1oxobutyl]amino]ethyl]thio]methyl]-7-[[7-[[[(11.beta.,17.alpha.)-9-fluoro11,17-dihydroxy-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]-1oxoheptyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

RN 389085-34-1 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-1-oxobutyl]amino]ethyl]thio]methyl]-7-[[8-[[[(11.beta.,17.alpha.)-9-fluoro-11,17-dihydroxy-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]-1-oxooctyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

$$\begin{array}{c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 389085-35-2 HCAPLUS

CN Androsta-1,4-diene-17-carboxamide, N-[[3-[[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]methyl]phenyl]methyl]-9-fluoro-11,17-dihydroxy-3-oxo-, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 389085-36-3 HCAPLUS

CN Androsta-1,4-diene-17-carboxamide, N-[10-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]decyl]-9-fluoro-11,17-dihydroxy-3-oxo-, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 389085-37-4 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[[3-[[[2-[[((11.beta.,17.alpha.)-9-fluoro-11,17-dihydroxy-3-

oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]methyl]phenyl]methyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 389085-39-6 HCAPLUS

CN Androsta-1,4-diene-17-carboxamide, N-[3-[3-[3-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]propoxy]propoxy]propyl]-9-fluoro-11,17-dihydroxy-3-oxo-, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 389085-41-0 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy l]-S-[8-[[2-[[((11.beta.,17.alpha.)-9-fluoro-11,17-dihydroxy-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]octyl]- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 389085-42-1 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy l]-S-[10-[[2-[[[(11.beta.,17.alpha.)-9-fluoro-11,17-dihydroxy-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]decyl]- (9CI) (CA INDEX NAME)

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L103 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:545747 HCAPLUS

DOCUMENT NUMBER:

135:133932

TITLE: An in vivo screen using chemical inducers of

dimerization

INVENTOR(S):

Cornish, Virginia W.

PATENT ASSIGNEE(S):

The Trustees of Columbia University in the City of New

York, USA

SOURCE:

PCT Int. Appl., 123 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                       KIND DATE
                                               APPLICATION NO. DATE
     WO 2001053355 A1 20010726 WO 2001-US2285 20010124
     WO 2001053355
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       A1 20021106 EP 2001-942644 20010124
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:
                                             US 2000-490320
                                                               W 20010124
                                             WO 2001-US2285
```

AB The subject of the invention provides a compd. having the formula: H1-X-B-Y-H2, wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. Said compds. can be called chem. inducers of dimerization. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage.

IT 282092-90-4 351419-37-9 351419-38-0 351419-39-1 351419-40-4 351419-41-5

351419-42-6 351419-43-7 351419-44-8

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(compds. comprising receptor-binding moiety, spacer and enzyme cleavable moiety for screening drugs and proteins capable of catalyze bond cleavage)

RN 282092-90-4 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy l]-S-[[3-[[[2-[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]methyl]ph enyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-37-9 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]amino]-1oxobutyl]amino]ethyl]thio]methyl]-7-[[7-[[[(11.beta.,16.alpha.,17.alpha.)9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17yl]carbonyl]amino]-1-oxoheptyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-38-0 HCAPLUS

CN Androsta-1,4-diene-17-carboxamide, N-[[3-[[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]methyl]phenyl]methyl]-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11.beta.,16.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-39-1 HCAPLUS

CN Androsta-1,4-diene-17-carboxamide, N-[10-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]decyl]-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11.beta.,16.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN

351419-40-4 HCAPLUS Androsta-1,4-diene-17-carboxamide, N-[5-[[4-[[(2,4-diamino-6-CNpteridinyl)methyl]methylamino]benzoyl]amino]pentyl]-9-fluoro-11,17dihydroxy-16-methyl-3-oxo-, (11.beta.,16.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-41-5 HCAPLUS

Androsta-1,4-diene-17-carboxamide, N-[3-[4-[3-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]propoxy]butoxy]propyl]-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11.beta.,16.alpha.,17.alpha.)-(9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-42-6 HCAPLUS

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
3-[[[2-[[(4S)-4-carboxy-4-[[4-[[(2,4-diamino-6pteridinyl)methyl]methylamino]benzoyl]amino]-1oxobutyl]amino]ethyl]thio]methyl]-7-[[8-[[[(11.beta.,16.alpha.,17.alpha.)9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17yl]carbonyl]amino]-1-oxooctyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 351419-43-7 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[8-[[2-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]octyl]- (9CI) (CA INDEX NAME)

RN 351419-44-8 HCAPLUS

CN L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy 1]-S-[10-[[2-[[[(11.beta.,16.alpha.,17.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]decyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L103 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:238920 HCAPLUS

DOCUMENT NUMBER:

133:86413

TITLE:

Dexamethasone-Methotrexate: An Efficient Chemical

Inducer of Protein Dimerization In Vivo

AUTHOR(S):

Lin, Hening; Abida, Wassim M.; Sauer, Robert T.;

Cornish, Virginia W.

CORPORATE SOURCE:

Department of Chemistry, Columbia University, New

York, NY, 10027, USA

SOURCE:

Journal of the American Chemical Society (2000),

122(17), 4247-4248

CODEN: JACSAT; ISSN: 0002-7863 American Chemical Society

DOCUMENT TYPE:

PUBLISHER:

Journal

English

LANGUAGE:

A heterodimeric dexamethasone-methotrexate compd. (Dex-Mtx) was prepd. that can dimerize proteins efficiently in vivo. A yeast three-hybrid system and a std. .beta.-galactosidase assay were used to show that Dex-Mtx (prepd. in 8 steps in 2% overall yield) can activate lacZ transcription in vivo.

ΙT 282092-90-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(dexamethasone-methotrexate: efficient chem. inducer of protein dimerization In vivo)

RN 282092-90-4 HCAPLUS

L-Homocysteine, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoy CN 1]-S-[[3-[[[2-[[(11.beta., 16.alpha., 17.alpha.)-9-fluoro-11, 17-dihydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl]carbonyl]amino]ethyl]thio]methyl]ph enyl]methyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

REFERENCE COUNT:

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT